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Komulainen, Kaisla

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RESEARCH ARTICLE

Childhood Psychosocial Environment and Adult Cardiac Health: A Causal Mediation Approach

Kaisla Komulainen, MA,[1,2] Murray A. Mittleman, MD, DrPH,[2,3] Saku Ruohonen, PhD,[4,5] Tomi T. Laitinen, MD, PhD,[4,6] Katja Pahkala, PhD,[4,6] Marko Elovainio, PhD,[1,7] Tuija Tammelin, PhD,[8] Mika Kähönen, MD, PhD,[9,10] Markus Juonala, MD, PhD,[11,12,13] Liisa Keltikangas-Järvinen, PhD,[1] Olli Raitakari, MD, PhD,[4,14] Laura Pulkki-Råback, PhD,[1] Markus Jokela, PhD[1]

Introduction: This study used causal mediation analysis to assess the life-course associations of a favorable childhood psychosocial environment with left ventricular mass and diastolic function in adulthood and the extent to which adult health behaviors mediate these associations.

Methods: The sample included 880 participants (56% women) from the Young Finns Study with data on the childhood environment from 1980, adult health behaviors (smoking, physical activity, diet, and BMI) from 2001 and an echocardiographic assessment of the left ventricular mass ($g/m^{2.7}$) and diastolic function (E/e' ratio; higher values indicating a lower diastolic function) from 2011. The associations of the childhood environment with the left ventricular mass and E/e' ratio and mediation pathways through health behaviors were assessed using marginal structural models that were controlled for age, sex, and time-dependent confounding by adult socioeconomic position (measured as educational attainment) via inverse probability weighting. The data were analyzed in 2018–2019.

Results: The mean age in 2011 was 41 (range 34–49) years. Those above versus below the median childhood score had a 1.28 $g/m^{2.7}$ lower left ventricular mass (95% CI= −2.63, 0.07) and a 0.18 lower E/e' ratio (95% CI= −0.39, 0.03). There was no evidence for indirect effects from childhood environments to left ventricular outcomes through adult health behaviors after controlling for time-dependent confounding by the adult socioeconomic position (indirect effect β= −0.30, 95% CI= −1.22, 0.63 for left ventricular mass; β= −0.04, 95% CI= −0.18, 0.11 for E/e' ratio). The results after multiple imputation were similar.

Conclusions: A favorable childhood environment is associated with more optimal cardiac structure and function in adulthood. After accounting for socioeconomic positions, adult health behaviors explain little of the associations.

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From the [1]Department of Psychology and Logopedics, Faculty of Medicine, University of Helsinki, Helsinki, Finland; [2]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts; [3]Cardiovascular Epidemiology Research Unit, Division of Cardiology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts; [4]Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku, Finland; [5]Orion Pharma, the Orion Corporation, Espoo, Finland; [6]Paavo Nurmi Centre, Sports and Exercise Medicine Unit, Department of Physical Activity and Health, University of Turku, Turku, Finland; [7]National Institute for Health and Welfare, Helsinki, Finland; [8]LIKES Research Center for Physical Activity and Health, Jyväskylä, Finland; [9]Department of Clinical Physiology, Tampere University Hospital, Tampere, Finland; [10]Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [11]Department of Medicine, University of Turku, Turku, Finland; [12]Division of Medicine, Turku University Hospital, Turku, Finland; [13]Murdoch Children's Research Institute, Parkville, Victoria, Australia; and [14]Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital, Turku, Finland

Address correspondence to: Laura Pulkki-Råback, PhD, Department of Psychology and Logopedics, Faculty of Medicine, University of Helsinki, PO Box 21 (Haartmaninkatu 3), 00014 University of Helsinki, Helsinki, Finland. E-mail: laura.pulkki-raback@helsinki.fi.

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INTRODUCTION

Although several studies have shown that early-life psychosocial adversity is associated with cardiovascular risks in adulthood,[1–3] recent studies have turned the focus toward favorable psychosocial factors that may help to maintain optimal cardiac health.[4–9] Adult cardiovascular health has been linked to various early-life psychosocial factors, including the family socioeconomic position (SEP),[10,11] emotional climate,[12,13] health behaviors,[14,15] environmental safety and stability,[2,16] and the self-regulation skills of the child.[4,17,18] In the Cardiovascular Risk in Young Finns Study, the cumulative presence of favorable psychosocial factors in childhood and adolescence was associated with a lower risk of Type 2 diabetes[9] and coronary artery calcification,[7] more optimal BMI development,[6] and a more ideal cardiovascular profile overall.[8] Similar findings have been reported in cohorts from the U.S.[4,12]

A favorable childhood environment may influence cardiovascular outcomes through direct biological pathways; for example, by supporting the optimal regulation of immune, metabolic, neuroendocrine, and autonomic nervous systems[19] and enhancing restorative physiological processes.[5] The childhood environment may also influence cardiovascular health through behavioral pathways. For instance, an adverse childhood environment has been associated with smoking, being overweight and physically inactive, and engaging in substance use in adulthood,[3,20] which in turn are associated with cardiovascular outcomes. If adult behavioral factors lie on the causal pathway from childhood conditions to later-life cardiovascular health, they can represent modifiable means to reverse the adverse effects of early-life circumstances. However, the degree to which the childhood environment causes adulthood cardiac outcomes through adult health behaviors is not well known.

This study extends previous studies by assessing the longitudinal associations of favorable childhood psychosocial environment with 2 established risk factors for cardiovascular morbidity and mortality: the adult left ventricular (LV) mass and LV diastolic function.[21–23] The aim was to identify potential behavioral mechanisms through which the childhood environment may be associated with adult cardiac outcomes. To this end, a counterfactual approach was used to assess whether ideal cardiovascular health behaviors in adulthood explain the associations of favorable childhood environment with more optimal LV mass and diastolic function.

METHODS

Study Sample

The Cardiovascular Risk in Young Finns Study is a prospective cohort study on the precursors of atherosclerosis among Finnish children and adolescents.[24] The initial sample included 3,596 participants aged 3–18 years in 1980. For this study, 2,067 individuals who had data on childhood psychosocial environment in 1980 were included. Of these 2,067 individuals, 864 were excluded because of missing behavioral and covariate (educational attainment) data in 2001, and an additional 323 were excluded owing to missing data on the LV mass and diastolic function in 2011, resulting in 880 participants. The study was conducted according to the Declaration of Helsinki and was approved by the Ethics Committee of the Hospital District of Southwest Finland. The Harvard T.H. Chan School of Public Health IRB reviewed this protocol and deemed this activity exempt under 45 CFR 46.101(b)(4). All participants gave written informed consent.

Measures

Echocardiograms were performed in 2011. Standard echocardiographic examinations[25,26] were produced from the standardized image planes and modes: parasternal long and short axis in two-dimensional and M-mode and apical four-chamber view.[25] The LV mass was calculated as $\text{LV mass(g)} = 0.8 \left(1.04\ [(\text{LV end–diastolic diameter} + \text{posterior wall thickness} + \text{interventricular septum thickness})^3 - \text{LV end–diastolic diameter}]^3\right) + 0.6$ g, and it was indexed by height raised to the allometric power of 2.7 (indexed LV mass = LV mass/height$^{2.7}$) as this indexation performs better in the context of individuals who were overweight and obese.[26,27] The LV diastolic function in the LV filling pressure was measured using the E/e' ratio (higher values indicate lower diastolic function), which was assessed with continuous and pulsed-wave Doppler measuring transmitral flow and tissue velocities.[25,26]

As described previously,[6–9] the childhood environment was assessed with 6 factors proposed as central components of childhood psychosocial environment[28,29]: socioeconomic environment, emotional environment, parental health behaviors, stressful events, the child's self-regulation, and social adjustment (Appendix Table 1, available online). These data were collected from parents of the study participants via questionnaires in 1980 (Appendix Table 2, available online). The 6 psychosocial factors were constructed from several dichotomous variables (0/1). For this purpose, the continuous data were first dichotomized. The selection of the cut offs is described in detail in Appendix Table 1 (available online). The scores from the 6 domains were standardized (z-scores) and then added together.[6–9] A favorable psychosocial factor score was treated both as a continuous score and a dichotomous variable with a cut off at the 50th percentile.

Four health behaviors—smoking, BMI, physical activity, and diet—were assessed in 2001 following the American Heart Association definitions of ideal cardiovascular health.[30] Smoking, physical activity, and diet were self-reported. The BMI (kg/m^2) was measured during a study visit. The total number of ideal behaviors was the count of the ideal scores on smoking (never smoked or quit >1 year ago), BMI (<25 kg/m^2), physical activity

(120 minutes/week moderate-intensity activity, 60 minutes/week vigorous-intensity activity, or a combination), and diet (2 of the 3 following components: fruits and vegetables every day, fish 2 or more times/week, and soft drinks 2 or fewer times/week).[30,31] A dichotomized measure of ideal cardiovascular behaviors (2 or more versus fewer than 2 ideal behaviors) was used in the analyses.

All the analyses were adjusted for sex and age. Self-reported educational attainment (highest level of educational attendance or completed education in 2001; dichotomized into no college versus college or higher) was used to assess the adult SEP.

STATISTICAL ANALYSIS

Linear regression analysis was used to examine the overall associations of the childhood psychosocial factors score with the LV mass and diastolic function. The LV mass and E/e' ratio were examined in separate models, both without adjustments and adjusted for age and sex. The childhood psychosocial score was first used as a continuous score, and the estimates were scaled to 1 SD of the score. The childhood score was then assessed as a dichotomous variable with a cut off at the median (50th percentile). The associations of the adult health behaviors with the LV mass and E/e' ratio were assessed in a separate linear regression analysis adjusted for age, sex, adult SEP, and the childhood score.

A counterfactual approach was used to assess the direct and indirect effects of the childhood environment on the LV outcomes through health behaviors in adulthood. The hypothetical causal model is presented in Figure 1. In this figure, a favorable psychosocial childhood environment is the exposure and ideal health behaviors the proposed mediator. Age and sex were included as potential confounders of both the exposure–outcome and the mediator–outcome associations.[32–38] In addition, the adult SEP was included as a potential exposure-induced confounder of the mediator–outcome association. This causal structure was hypothesized based on the established associations of the childhood psychosocial environment with the adult SEP and the associations of the adult SEP with both health behaviors and LV structure and function.[39–41]

In the presence of exposure-induced confounding, natural direct and indirect effects are not identified, but randomized interventional analogs for natural direct and indirect effects can be estimated.[42,43] In this study, exposure-induced confounding was controlled in marginal structural models by inverse probability weighting following the approach described by VanderWeele et al.[43] The weights were constructed based on logistic regression models for the childhood psychosocial environment, adult SEP, and ideal health behaviors (all treated as dichotomous variables), and the estimates of direct and indirect effects were obtained from weighted linear regression models regressing the LV outcomes on the exposure. The effect decomposition has been described previously.[43] The SEs and CIs were obtained with robust variance estimation to account for the sampling error in estimating the weights.[44] The LV mass and E/e' ratio were analyzed in separate models.

Multiple imputation with chained equations was performed to account for missing data (Appendix Table 3, available online).[45] The imputation model included the measures of LV mass; E/e' ratio; educational attainment in 2001, 2007, and 2011; ideal health behaviors in 1986, 2001, 2007, and 2011; sex; age; and childhood psychosocial factors in 1980. All the study variables with missing data were imputed, and all the analyses were repeated in 10 imputed data sets. The 6 childhood psychosocial factors were imputed as separate variables. Participants with imputed outcomes were excluded from the analysis of imputed data.[45] As sensitivity analyses, all the analyses were repeated with data on health behaviors and education assessed in 2007. Additionally, the analyses were conducted after participants with self-reported diagnoses of cardiac disease or events in 2001 had been excluded.

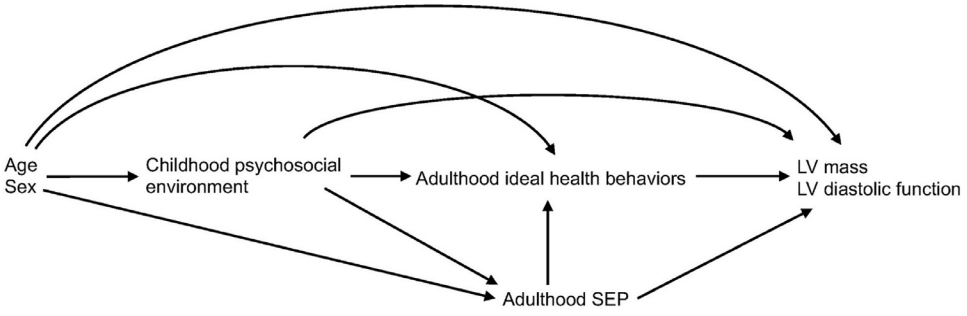

Figure 1. Directed acyclic graph depicting the conceptual model of the relationships between the childhood environment, health behaviors, and SEP in adulthood and the outcomes of LV mass and diastolic function.
LV, left ventricular; SEP, socioeconomic position.

Finally, mediation was assessed through each health behavior separately. All the analyses were conducted in Stata, version 13.1 in 2018–2019.

RESULTS

Table 1 and Appendix Table 4 (available online) show the sample characteristics. Compared with those excluded owing to missing data, the included participants were almost 1 year older, more often female (56% vs 48%), and from more favorable childhood psychosocial environments (mean, 0.7 vs 0.4) (Appendix Table 5, available online). Descriptive statistics after multiple imputations are presented in Appendix Table 6 (available online).

Table 1. Characteristics of 880 Participants From the Cardiovascular Risk in Young Finns Study

Characteristics	Mean (SD)	*n* [%]	*n*
Age (years) in 2011	41.4 (4.9)	—	880
Sex (female)	—	493 [56]	880
Educational attainment in 2001	—	—	880
No college	—	616 [70]	—
College or higher	—	264 [30]	—
Psychosocial factors in 1980	—	—	—
Favorable socioeconomic environment (range, 0–4)	1.7 (1.2)	—	880
Favorable emotional environment (range, 0–4)	2.5 (0.9)	—	880
Favorable health behaviors of parents (range, 0–6)	4.9 (1.1)	—	880
Lack of stressful events (range, 0–5)	4.8 (0.5)	—	880
High self-regulatory behavior (range, 0–7)	6.7 (0.7)	—	880
High social adjustment (range, 0–2)	1.5 (0.7)	—	880
Childhood psychosocial factors score	0.7 (2.6)	—	880
Ideal health behaviors in 2001	—	—	880
≥2 ideal behaviors	—	613 [70]	—
<2 ideal behaviors	—	267 [30]	—
Nonsmoking	—	608 [69]	—
BMI <25 kg/m^2	—	519 [59]	—
Ideal physical activity	—	480 [55]	—
Ideal diet	—	231 [26]	—
Left ventricular mass (g/m$^{2.7}$)	30.4 (6.7)	—	853
E/e' ratio	4.8 (1.0)	—	860

Note: All the values except for the left ventricular mass and E/e' ratio were calculated for participants with data on the LV mass, E/e' ratio, or both. The mean left ventricular mass (g/m$^{2.7}$) 29.6 (SD=6.2) and 31.2 (7.1) among those above vs below the median of the childhood psychosocial score. The mean E/e' ratio 4.7 (0.9) versus 4.9 (1.0) among those above versus below the median of the childhood psychosocial score.

Unadjusted linear regression analyses showed that the favorable childhood psychosocial score was associated with a lower LV mass and E/e' ratio. A 1-SD difference in the childhood psychosocial score was associated with a 0.83 g/m$^{2.7}$ difference in the LV mass (95% CI= −1.27, −0.38) and a 0.08 difference in the E/'e ratio (95% CI= −0.15, −0.01). These associations remained significant after adjusting for age and sex (β= −0.66, 95% CI= −1.09, −0.23 for LV mass; β= −0.08, 95% CI= −0.15, −0.02 for E/'e ratio) and age, sex, and adult SEP (β= −0.52, 95% CI= −0.96, −0.08 for LV mass; β= −0.08, 95% CI= −0.15, −0.02 for E/'e ratio). Of the 6 psychosocial factors, the socioeconomic environment, parental health behaviors, and child's self-regulatory behavior were associated with LV outcomes (Appendix Table 7, available online). The associations of the childhood psychosocial score with the LV mass and E/e' ratio did not differ according to age (psychosocial score by age interaction: p=0.79 for LV mass, p=0.63 for E/e' ratio) or sex (psychosocial score by sex interaction: p=0.52 for LV mass, p=0.34 for E/e' ratio). Those with a childhood psychosocial score above the median had 84% higher sex- and age-adjusted odds for having 2 or more ideal health behaviors in adulthood compared with those below the median (OR=1.84, 95% CI=1.35, 2.51). Having 2 or more ideal health behaviors in adulthood was associated with a 2.17 g/m$^{2.7}$ lower LV mass (95% CI= −3.14, −1.20) and a 0.23 lower E/e' ratio (95% CI= −0.38, −0.09) compared with having fewer than 2 ideal behaviors after adjusting for sex, age, childhood psychosocial environment, and adult SEP.

Differences in the LV mass and E/e' ratio above and below the median of the childhood psychosocial score are presented in Table 2. The age- and sex-adjusted differences from the linear regression models coincided with the total effect estimates from the marginal structural models that were controlled for age, sex, and time-dependency confounding by the adult SEP (total effect β= −1.28, 95% CI= −2.63, 0.07 for LV mass; β= −0.18, 95% CI= −0.39, 0.03 for E/e' ratio). The marginal randomized interventional analog of the direct effect indicated a difference of 0.98 g/m$^{2.7}$ in the LV mass among those above the median of the childhood score versus those below the median (95% CI= −1.97, 0.00). The analog for the direct effect on the LV diastolic function indicated a corresponding difference of 0.14 in the E/e' ratio (95% CI= −0.29, 0.01). Approximately 23% and 21% of the associations of childhood environment with the LV mass and E/e' ratio were estimated to be mediated through adult health behaviors (β= −0.30, 95% CI, −1.22, 0.63 for LV mass; β= −0.04, 95% CI= −0.18, 0.11 for E/e' ratio). However, these estimates were not statistically significant (natural indirect effect: p=0.53 for

Table 2. Differences in LV Outcomes Between Those Above and Below the Median of Childhood Psychosocial Score

Model	Complete cases		Multiple imputation	
	LV mass ($g/m^{2.7}$) Difference (95% CI)	E/e' ratio Difference (95% CI)	LV mass ($g/m^{2.7}$) Difference (95% CI)	E/e' ratio Difference (95% CI)
Linear regression				
Unadjusted	−1.61 (−2.51, −0.71)	−0.15 (−0.28, −0.02)	−1.67 (−2.34, −1.01)	−0.17 (−0.26, −0.07)
Sex- and age-adjusted	−1.16 (−2.02, −0.29)	−0.16 (−0.29, −0.03)	−1.37 (−2.01, −0.72)	−0.16 (−0.25, −0.06)
Marginal structural model[a]				
Total effect	−1.28 (−2.63, 0.07)	−0.18 (−0.39, 0.03)	−1.36 (−2.27, −0.44)	−0.17 (−0.31, −0.03)
Direct effect	−0.98 (−1.97, 0.00)	−0.14 (−0.29, 0.01)	−1.05 (−1.74, −0.36)	−0.14 (−0.25, −0.04)
Indirect effect	−0.30 (−1.22, 0.63)	−0.04 (−0.18, 0.11)	−0.31 (−0.90, 0.29)	−0.02 (−0.12, 0.07)

Note: Sample sizes differ owing to the available data (n=853 for LV mass, n=860 for E/e' ratio in the complete case analysis, n=1,908 for the LV mass, n=1,939 for the E/e' ratio after multiple imputation). In the complete case analysis, those above the median of the childhood psychosocial score had a 0.90 $g/m^{2.7}$ lower LV mass (95% CI= −1.78, −0.02) and a 0.16 lower E/e' ratio (95% CI= −0.29, −0.03) compared to those below the median of the childhood score after adjusting for age, sex, and adult SEP. In the analyses with imputed data, those above the median of the childhood psychosocial score had a 1.16 $g/m^{2.7}$ lower LV mass (95% CI= −1.34, −0.99) and a 0.15 lower E/e' ratio (95% CI= −0.18, −0.12) compared to those below the median of the childhood score after adjusting for age, sex, and adult SEP.
[a]Estimates from the marginal structural model adjusted for age, sex, and time-dependent confounding by adult SEP.
LV, left ventricular; SEP, socioeconomic position.

the LV mass, p=0.61 for the E/e' ratio) (Table 2). Results with imputed data concurred with those from the primary analyses (Table 2). Although the estimates for LV mass were somewhat greater, no indirect effects were observed in the imputed data.

In the complete case analysis using health behavior and educational data from 2007, all the associations were somewhat stronger for the LV mass and weaker for the E/e' ratio compared with the primary analysis, but no indirect associations were observed (Appendix Table 8, available online). Imputed analyses with data from 2007 yielded similar results to those from the imputed analyses with data from 2001 (Appendix Table 8, available online). All the results were substantially similar after excluding the participants with cardiac disease or events (Appendix Table 9, available online). No indirect associations were seen in the analyses that estimated the indirect effect through each health behavior separately (Appendix Table 10, available online).

DISCUSSION

This prospective cohort study found that a favorable psychosocial environment in childhood and youth is associated with better cardiovascular health 31 years later, as measured by the cardiac structure (LV mass) and diastolic function (E/e' ratio). Compared with those with childhood psychosocial scores below the median, those above the median had a 1.2 $g/m^{2.7}$ lower LV mass and 0.2 lower E/e' ratio. After accounting for the adult SEP, there was no consistent evidence of health behaviors mediating the association of childhood psychosocial environment with the LV mass and E/e' ratio; the associations of childhood environment are explained largely by other factors besides ideal health behaviors.

Previous studies have demonstrated the associations of psychosocial factors in childhood with several important cardiometabolic risk factors in adulthood.[4,6–9,12] This study extends these findings to the LV mass and diastolic function. Increased LV mass and LV diastolic dysfunction measured as the LV filling pressure have been found to be prognostic of the risk of cardiovascular events and premature morbidity, independent of cardiovascular comorbidities and beyond traditional risk factor assessment, and thus, they are clinically relevant markers for cardiovascular risk stratification.[21–23] A 1 $g/m^{2.7}$ increase in the LV mass has been associated with a 40% increased rate of adverse cardiovascular events.[46] In this study, the difference between those with unfavorable versus favorable childhood scores was 1.2 $g/m^{2.7}$, which would correspond to a 3% higher rate of cardiovascular events. Although the incubation time from childhood exposures to disease manifestation may be long, some evidence suggests that childhood psychosocial exposures are associated with progression of cardiovascular risk factors over time.[2,6] Future studies with repeated measurements of cardiac structure and function are needed to elucidate the timing of etiologically relevant pathophysiological changes.

Several pathways can connect childhood environment with adulthood cardiac health. Childhood and youth are developmental periods during which important regulatory systems and physiological responses are programmed.[19,47] The childhood psychosocial environment may initiate differences in immune, metabolic, neuroendocrine, and autonomic nervous systems relevant to cardiovascular health across life.[19] Behavioral factors are suggested as

a potentially important, modifiable mechanism explaining the association of childhood psychosocial environment with cardiovascular outcomes.[3,5,19] However, the extent to which this occurs is not well understood.[19] This study used marginal structural models to assess the associations of childhood environment with adult cardiac outcomes through ideal cardiovascular health behaviors while controlling for time-dependent confounding by the adult SEP. After accounting for age, sex, and adult SEP, there was no evidence of an indirect association of the childhood environment with the LV mass and diastolic function through ideal cardiovascular health behaviors. Nevertheless, health behaviors are considered a major contributor to the socioeconomic gradient in health. A pathway from the childhood environment to the LV mass and diastolic function may involve a sequence of exposures,[47] whereby the childhood environment influences the adult SEP, which in turn drives the association of health behaviors with cardiac outcomes. This is feasible given that some evidence suggests an indirect association from childhood environment to adult cardiovascular outcomes through the adult SEP.[12,16] Furthermore, a recent study examining the associations of childhood psychosocial adversity with adult cardiac outcomes suggested an indirect association through health behaviors.[16] A relevant question is whether favorable and adverse childhood exposures tap into different intermediate mechanisms, with the role of health behaviors possibly accentuating those associated with childhood adversity. Further work recognizing potentially distinct pathways initiated by favorable versus adverse early-life exposures is needed to explain the psychosocial origins of lifetime cardiovascular health. Future research should also evaluate the degree to which standard cardiovascular risk factors, for example, blood pressure or insulin resistance, may explain the associations of childhood psychosocial environment with adult cardiac structure and function.

Limitations

The assessment of mediation in a life-course perspective using longitudinal observational designs is complex. For the estimates of direct and indirect effects to have a causal interpretation, strong assumptions regarding confounding are needed.[42,43] In particular, longitudinal settings often involve long time intervals between measurements of the exposure and the mediator. This introduces the possibility of intermediate, time-dependent confounding of the mediator–outcome association.[42] In this study, time-dependent confounding was addressed using a recently developed method for the effect decomposition in the causal mediation framework. This approach is based on inverse probability weighting in marginal structural models, which requires estimating additional parameters, inevitably decreasing its statistical power. The precision of the estimates obtained from this analysis thus may be compromised by the methodological approach that was chosen to accurately represent the underlying causal structure.

Some other limitations should be noted. The analysis is based on observational data, and the possibility of residual or unmeasured confounding cannot be ruled out. Causal mediation analysis helped to improve the specification of the causal model, although the variables were dichotomous, which decreased the precision of measurement.[48] This study is a long-running cohort study, and loss to follow-up cannot be avoided. The complete case and multiple imputation analyses gave similar results for the lack of indirect effect through health behaviors, but it is possible that selective loss to follow-up biased the estimates. Although no established standard currently exists for measuring childhood psychosocial environment, the 6 included factors are theoretically sound[28,29] and have been associated with relevant cardiometabolic outcomes.[2,4,10–18] Likewise, no clear cut offs exist for defining favorable versus adverse psychosocial experiences, and the childhood score cannot fully differentiate the relative contributions of the beneficial versus the adverse aspects of childhood environment. Although the diet was measured using validated food frequency questionnaires, and the physical activity questionnaire has shown acceptable convergent validity against pedometric data,[49–51] self-reported health behaviors involve a risk of reporting bias based on childhood background or adult SEP. Finally, the participants were a white, ethnically homogeneous cohort residing in Finland, which limits the generalizability of these findings. The strengths of this study include prospective, encompassing data on childhood psychosocial circumstances and the application of recently developed methods to assess mediation.

CONCLUSIONS

This study found that a favorable childhood environment is associated with more optimal LV mass and diastolic function in adulthood. Findings from the causal mediation analysis suggest that this association is not explained by ideal cardiovascular health behaviors in adulthood once age, sex, and adult SEP are accounted for. Currently, these results highlight the importance of early-life environments in initiating the pathways of long-term cardiovascular health, and motivate the further application of rigorous designs to assess the causal pathways from childhood psychosocial environment to adult cardiovascular endpoints.

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SUPPLEMENTAL MATERIAL

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